THE EFFECTS OF HYPOPHYSECTOMY ON INTELLECTUAL FUNCTIONING*

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THE purpose of the present study was to evaluate the effects of hypophysectomy, the surgical removal of the pituitary gland, on the intellectual functioning of the individuals undergoing this particular form of surgery.

The pituitary gland, which is located at the base of the midbrain, is believed to control the activities of all other endocrine glands. Hypophysectomy is now performed in an attempt to induce remission of certain cancers suspected to be dependent upon endocrine gland factors (7). Luft and Olivecrona reported a survival duration of 3–28 months in patients with metastatic breast cancer who had undergone hypophysectomy (3). Ray and Pearson (10) reported an average remission of the disease of 7 months for the total group studied, with 22 months after surgery being the longest time of remission noted. Following hypophysectomy a deficiency state is created on all hormonal products of the pituitary gland. This type of hormonal deprivation is at present applied only to the advanced stages of cancer but the possibility exists that hypophysectomy may eventually become the preferred initial endocrine treatment for metastatic breast cancer (6). Ray suggests that even if hypophysectomy is not employed as the initial surgical procedure in altering the hormonal environment, it may be preferable to adrenalectomy as a second operation following castration (10).

When the first reports on hypophysectomy were received, some doubts were raised as to the value of this procedure. It was speculated that patients undergoing this type of surgery might become intellectually so deteriorated afterwards that the benefit of the prolongation of the lifespan might be offset by the possible mental incapacity. In addition, it was observed that most of the patients themselves who were faced with this type of surgery raised the question as to the possibility of mental deterioration following hypophysectomy. All these considerations gave the impetus to the present study.

Hypophysectomy involves two variables: (1) brain surgery, and (2) the elimination of the major source of endocrine stimulation and hormone production. A number of studies have reported impairment in intelligence, reasoning, and abstract functions resulting from frontal lobe defects. Rylander (11), Koskoff (2), Malmo (4), and Petrie (8) confirmed this contention. Damage to the frontal lobes by means of frontal lobotomy resulted in an impairment of

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intellectual functioning. In the present series of patients no lobotomy was performed; only a manipulation of the frontal lobe occurred. The frontal lobe was retracted in order to gain access to the pituitary gland (7). With respect to the endocrinological influence, Timme has already reported (12) that patients suffering from hypopituitarism give the impression of being mentally retarded though they are usually of normal or above normal intelligence. Timme believes that this impression is created because of their slowness of responses.

On the basis of these findings in the literature, it was hypothesized that hypophysectomy will not effect any significant changes in intellectual functioning, nor will it result in brain damage.

Procedure

Twenty white female patients, ranging in age from 40–66 years, who were suffering from metastatic malignant breast tumours suspected to be dependent upon endocrine gland factors were studied before and after hypophysectomy. All patients were tested with the Wechsler-Bellevue Intelligence Scale pre-operatively and 6–10 weeks post-operatively. This time interval was chosen as after a period of one month the patients are considered stabilized from a physiological point of view, and also in order to retest the patients as long as most of the pituitary hormones were still eliminated. Following hypophysectomy the hormones which are absolutely necessary for the maintenance of the functions of the living body are replaced. Thus, the hormone cortisone was administered just prior to, during, and immediately after surgery, while thyroid substitution hormones were administered later as the necessity arose. Hypothyroidism usually develops within 4–8 weeks following hypophysectomy and thyroid preparations were administered as soon as advanced features of thyroid deficiency were noted (7).

The Wechsler-Bellevue Intelligence Scale consists of a Verbal scale and a Performance scale. The Verbal scale consists of subtests which tap general information, memory for digits forward and backward, a similarity test which assesses the subject's logical thinking, a comprehension test which reveals the subject's ability to deal with practical situations, an arithmetic reasoning test, and, as an alternative, a vocabulary test.

The Performance scale includes the Picture Completion test, which measures the subject's ability to differentiate essential from unessential details, the Block-Design test, which reveals a number of temperamental traits, shows up mental deterioration and disturbances in the higher perceptual processes, the Object Assembly test, which reveals the subject's method of perception, the degree to which he relies on trial and error, and how he reacts to his mistakes, and the Digit Symbol test, which reveals the motor set and speed of the subject (13).

The Intelligence scale was administered and scored in the usual manner, according to Wechsler's Manual (13). Whenever any of the subtests had to be omitted for any reason, the scores were prorated in order to obtain an I.Q. The Verbal I.Q., the Performance I.Q., and the Full Scale I.Q. were calculated separately. The mean I.Q.s before surgery and after hypophysectomy were determined for the 20 patients and a t-test was applied in order to evaluate the statistical significance of the difference of the means obtained. As the means to be compared are based on the same individuals, the test of significance had to make allowance for the fact that the two sets of measurements were obtained from the same subjects and, therefore, not random with respect to each other.

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Therefore, the difference between correlated means was calculated according to McNemar and the special formula for the standard error of the mean difference for small samples was used (5, p. 126). A t-value of at least 2·093 was considered significant at the ·05 level of confidence.

It was reasoned that, though the overall I.Q. might not reveal any change after surgery, nevertheless, some changes might have occurred in the various subtests on the basis of which the I.Q.s were calculated. Therefore, the raw scores of each pre- and post-operative subtest were submitted to a statistical test of significance as described above.

In order to assess whether intellectual impairment had occurred as a result of brain damage following hypophysectomy, two methods were used. (1) Certain subtests of the Wechsler-Bellevue Scale which are considered as diagnostic indicators of brain damage were carefully evaluated. Wechsler states that, in general, the symptoms of brain damage are "disturbances in the visual motor spheres, a loss of shift, various memory defects, and a falling off of capacities involving organization and synthetic ability" (13, p. 153). Wechsler believes that there is a constant falling off of the scores on the following subtests: Block Design, Digit Symbol, Arithmetic, Memory for Digits Backwards, Similarities, and possibly Object Assembly. Therefore, special emphasis was given to the scores of these subtests. Most of the investigators using the Wechsler-Bellevue Scale with brain-injured patients noted a severe impairment of their performance on the Block Design test (1, p. 115). (2) The "differential-test-score method" for measuring mental deterioration was applied. This method is based on the normal decline of intellectual functioning with age. A certain degree of mental deterioration is expected with advancing age. However, if this degree exceeds the one of normal deterioration, it is considered pathological (13, p. 63). The "per cent loss of mental deterioration" was calculated for the pre- and post-operative group.

The same statistical procedure as outlined above was applied to both methods in order to assess the significance of intellectual impairment as a reflection of brain damage incurred during the surgical procedure.

No adequate control group could be obtained for this experiment. The ideal control group would have been a series of similar cancer patients undergoing the same surgical procedure as in hypophysectomy without having the pituitary gland removed. However, for obvious reasons, this was not possible. It was, therefore, decided to compare the results of this study with the findings on the effects of brain surgery as reported in the literature.

Results

In general, no statistically significant changes could be noted between pre- and post-operative intellectual functioning. The mean pre-operative Verbal I.Q. was 103 and the mean post-operative Verbal I.Q. was 102·2. On the Performance scale a mean I.Q. of 101·4 was obtained pre-operatively and the post-operative mean was 103·1. The pre-operative Full Scale I.Q. showed a mean of 102·8 and the post-operative mean 103·1. Neither the Verbal I.Q., nor the Performance I.Q., nor the Full Scale I.Q. changed significantly as a result of hypophysectomy for the group as a whole. Also, no significant difference occurred on the raw scores of the various subtests except in two; the subtests "Information" and "Picture Completion" showed a post-operative significant increase in raw scores. Though no significant difference in the raw scores could be noted on the subtest "Block Design", which is considered an

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excellent test of general intelligence, nevertheless, the time necessary, as measured in seconds, to complete the various block designs showed a significant post-operative increase. These findings are illustrated in Table I.

TABLE I

Significance of Difference Between Pre- and Post-operative Measurements on the Wechsler-Bellevue Intelligence Scale in the Hypophysectomy Group

Measurement	t-value
Verbal I.Q.	·82
Performance I.Q.	1·33
Full scale I.Q.	·293
Information	2·18*
Digit span	·376
Comprehension	1·74
Arithmetic	·308
Similarities	·65
Vocabulary	·81
Picture completion	2·2*
Block design	1·25
Object assembly	·825
Digit symbol	1·072
Time needed on Block design	3·23*

* Significant at the 0·5 level of confidence.

An examination of the pre- and post-operative raw scores of the subtests considered indicators for brain damage revealed that no significant change has occurred post-operatively in this respect. Furthermore, the difference between the pre- and post-operative "per cent. loss of mental deterioration", another indicator of brain damage, showed that no significant change could be noted post-operatively. These data are compiled in Table II.

TABLE II

Significance of Difference Between Pre- and Post-operative Measurements on the Indicators for Brain Damage

Indicator	t-value
Block design	1·25
Digit symbol	1·072
Arithmetic	·308
Digits backward	1·143
Similarities	·65
Object assembly	·825
Per cent. loss of mental deterioration	·555

A t-value of at least 2·093 is considered significant at the ·05 level of confidence. None of the above t-values is significant.

From the above results it appears that our hypothesis is confirmed. No significant changes seem to have occurred in intellectual functioning and no measurable brain damage, as determined by the tests, could be noted as a result of hypophysectomy in the patients under study. However, a significant increase in general information and the ability to distinguish the essential from non-essential details, i.e. in the power of observation and in accuracy, seem to have occurred. Furthermore, a significant increase in the time necessary to perform on a test which requires a simultaneous performance of visual and motor abilities could be noted.

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Discussion

The connection of the pituitary gland to other areas of the brain is not well understood—whether impulses are transmitted from the more distant brain centres to the pituitary gland or vice versa. From the above results, one can conclude, in general, that the pituitary gland does not seem to have any influence on the intellectual functioning of the individual. It also appears that the severance of the fibres which might connect the pituitary gland with those regions of the cortex of the brain which are generally considered as the centres of the individual's reasoning power and abstract ability, has no effect on the adequate functioning of the intellect.

A comparison of the results of the present experimental group with the findings in the literature, which report the effect of brain surgery on non-psychotic patients, reveals that mere manipulation of the frontal lobe, which is involved in hypophysectomy, does not result in decreased intellectual functioning, while lobotomy effects a significant decrease in general intelligence.

Rylander (11) studied six cases, who suffered from different types of severe neuroses, on whom frontal lobotomy was performed as the choice of treatment. He reported a significant mean I.Q. decrease of 11·6 points on the Stanford Binet test in five cases. Malmo (4) reports a significant post-operative mean decrease of 8·3 points of I.Q. on the Wechsler-Bellevue Scale in six neurotic patients on whom frontal lobotomy and frontal gyrectomy was performed. Koskoff and his associates (2) studied seven cases on whom frontal lobotomy was performed for the alleviation of intractable pain. They report a post-operative mean decline of 20·4 points of the Full Scale I.Q. in five cases. Petrie (8) reports, in 20 neurotic patients on whom a prefrontal leucotomy was performed, a significant post-operative decrease of 5 points on the Full Scale I.Q. on the Wechsler-Bellevue Scale. She also noted a decrease in accuracy and an increase in speed in some of the special tests she used to evaluate temperament (9). In the present study, a significant increase in accuracy and a significant decrease in speed could be observed post-operatively. Petrie attributes her findings partly to a change in temperament post-operatively. She believes that the post-leucotomy patients show a decrease in neuroticism which also affected the performance on the intelligence test. She feels that the neurotic is slower and more accurate because of his disposition to rigidity and deliberation.

In line with Petrie's assumptions, it appears that the improvement in accuracy and the decrease in speed in the present experimental group could possibly be the result of an increased "neuroticism", due to the elimination of the hormones; however, it seems to this investigator that the patients exhibited a greater degree of accuracy post-operatively, possibly because they experienced an improved sense of physical well being after surgery. The significant increase in accuracy ("Information" and "Picture Completion") may also be simply the result of the practice effect gained through retesting. The decrease in speed appears to be related to the effects of the elimination of the thyrotropic hormones, i.e. the slowness in response may be attributed to a secondary hypothyroidism resulting from the pituitary deficiency.

Summary

1. The intellectual functioning of twenty white female patients, suffering from metastatic breast cancer, who underwent hypophysectomy as a therapeutic measure to check the progress of the disease, were studied pre- and post-operatively.

2. It was hypothesized that hypophysectomy will have no effect on the intellectual functioning of the individuals under study and that no brain damage will occur as a result of this surgery.

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3. No statistically significant change in general intellectual functioning and no brain damage, as measured by the tests, could be noted post-hypophysectomy. Thus, the hypothesis was confirmed.

4. An increase in accuracy, possibly as a result of a post-operative improvement in health or due to the practice effect involved in re-testing, and a decrease of speed, probably related to a secondary hypothyroidism because of a deficiency of pituitary hormones, could be noted.

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